Amendments to the Claims

1-19 (Canceled)

20. (Previously presented) A nucleic acid molecule comprising an open reading frame encoding a cleavable single-chain polypeptide, said open reading frame comprising:

a) a first nucleotide sequence encoding at least a portion of a clostridial neurotoxin heavy chain binding element able to preferentially interact with a target cell surface marker under physiological conditions;

b) a second nucleotide sequence encoding at least a portion of a clostridial neurotoxin heavy chain translocation element able to facilitate the transfer of said single-chain polypeptide across a vesicular membrane;

c) a third nucleotide sequence encoding at least a portion of a therapeutic element peptide having biological activity when released into the cytoplasm of the target cell, and

d) a fourth nucleotide sequence encoding a peptide comprising a non-native Clostridial neurotoxin protease cleavage site;

wherein said fourth nucleotide sequence intervenes between said second sequence and said third nucleotide sequence.

21. Previously presented) The molecule of claim 20, wherein said open reading frame further comprises a fifth nucleotide sequence encoding a peptide comprising a target-binding portion of a binding tag.

22. (Previously presented) The molecule of claim 21, wherein said target-binding portion comprises a His_6, a monoclonal antibody, a maltose binding protein, a glutathione-S-transferase, a protein A, or a calmodulin binding protein.

23. (Previously presented) The molecule of claim 20, wherein said binding element is a *Clostridium botulinum* neurotoxin heavy chain.

24. (Previously presented) The molecule of claim 20, wherein said translocation element is a *Clostridium botulinum* neurotoxin heavy chain.

25. (Previously presented) The molecule of claim 20, wherein said translocation element is a *Clostridium tetani* neurotoxin heavy chain.

26. (Previously presented) The molecule of claim 20, wherein said therapeutic element peptide comprises a clostridial neurotoxin light chain.

27. (Previously presented) The molecule of claim 26, wherein said clostridial neurotoxin light chain is a *Clostridium botulinum* neurotoxin light chain.

28. (Previously presented) The molecule of claim 26, wherein said clostridial neurotoxin light chain is a *Clostridium tetani* neurotoxin light chain.

29-31. (Canceled)

32. (Currently amended) A method of making a cleavable single-chain polypeptide comprising:

a) inserting the ~~plasmid~~ nucleic acid molecule of any one of claims 20-28, 31 or 38 into a suitable host cell,
b) growing said host cell in culture, and
c) permitting or inducing the host cell to express the single chain polypeptide encoded by said plasmid.

33. (Currently amended) A method of purifying a cleavable single chain polypeptide comprising:

a) lysing a host cell expressing a single chain polypeptide from the ~~plasmid~~ nucleic acid molecule of either of claim 21 or 22 to produce a cell lysate,
b) contacting said cell lysate with a target compound so as to form a specific binding complex capable of being immobilized comprising said binding tag and said target compound, and
c.) separating said binding complex from said cell lysate.

34-37. (Canceled)

38. (Previously presented) The molecule of claim 20, wherein said binding element is a *Clostridium tetani* neurotoxin heavy chain.

39. (Currently amended) The molecule of claim 20, wherein said protease cleavage site ~~comprising~~comprises SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 22 or SEQ ID NO: 23.

40. (Previously presented) A nucleic acid molecule comprising an open reading frame encoding a cleavable single-chain polypeptide, said open reading frame comprising:

a) a first nucleotide sequence encoding at least a portion of a binding element peptide able to preferentially interact with a sensory afferent neuron cell surface marker under physiological conditions;

b) a second nucleotide sequence encoding at least a portion of a clostridial neurotoxin heavy chain translocation element able to facilitate the transfer of said single-chain polypeptide across a vesicular membrane;

c) a third nucleotide sequence encoding at least a portion of a clostridial neurotoxin light chain therapeutic element having biological activity when released into the cytoplasm of said target cell; and

d) a fourth nucleotide sequence encoding a peptide comprising a non-native Clostridial neurotoxin protease cleavage site;

wherein said fourth nucleotide sequence intervenes between said second sequence and said third nucleotide sequence.

41. (Previously presented) The molecule of claim 40, wherein said open reading frame further comprises a fifth nucleotide sequence encoding a peptide comprising a target-binding portion of a binding tag.

42. (Previously presented) The molecule of claim 41, wherein said target-binding portion comprises a His_6, a monoclonal antibody, a maltose binding protein, a glutathione-S-transferase, a protein A or a calmodulin binding protein.

43. (Previously presented) The molecule of claim 40, wherein said translocation element is a *Clostridium botulinum* neurotoxin heavy chain.

44. (Previously presented) The molecule of claim 40, wherein said translocation element is a *Clostridium tetani* neurotoxin heavy chain.

45. (Previously presented) The molecule of claim 40, wherein said therapeutic element is a *Clostridium botulinum* neurotoxin light chain.

46. (Previously presented) The molecule of claim 40, wherein said therapeutic element is a *Clostridium tetani* neurotoxin light chain.

47. (Currently amended) The molecule of claim 40, wherein said protease cleavage site ~~comprising~~comprises SEQ ID NO: 15, SEQ ID NO: 16, SEQ ID NO: 22 or SEQ ID NO: 23.